PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference UCL-052-PCT	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. PCT/EP 02/02505	International filing date *(day/month/year)* 07.03.2002	Priority date *(day/month/year)* 07.03.2002
International Patent Classification (IPC) or both national classification and IPC C12Q1/68		
Applicant UNIVERSITE CATHOLIQUE DE LOUVAIN et al.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 7 sheets, including this cover sheet.

   ☐ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the opinion
   - II ☐ Priority
   - III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - IV ☐ Lack of unity of invention
   - V ☒ Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
   - VI ☐ Certain documents cited
   - VII ☐ Certain defects in the international application
   - VIII ☐ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
01.10.2003	20.04.2004
Name and mailing address of the international preliminary examining authority: European Patent Office - P.B. 5818 Patentlaan 2 NL-2280 HV Rijswijk - Pays Bas Tel. +31 70 340 - 2040 Tx: 31 651 epo nl Fax: +31 70 340 - 3016	Authorized Officer Gabriels, J Telephone No. +31 70 340-4282

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/EP 02/02505

I. Basis of the report

1. With regard to the **elements** of the international application *(Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17))*:

Description, Pages

1-33 as originally filed

Claims, Numbers

1-19 as originally filed

Drawings, Sheets

1/7-7/7 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in written form.
- ☐ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- ☐ the description, pages:
- ☐ the claims, Nos.:
- ☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)).

   (Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

   ☐ the entire international application,

   ☒ claims Nos. 1-5,7,9,16,19 (all partially) 11-15 (all completely)

   because:

   ☒ the said international application, or the said claims Nos. 1-4 (with respect to IA) relate to the following subject matter which does not require an international preliminary examination (specify):

   see separate sheet

   ☐ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. are so unclear that no meaningful opinion could be formed *(specify)*:

   ☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

   ☒ no international search report has been established for the said claims Nos. 1,5,7,9,16,19 (all partially) 11-15 (all completely)

2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

   ☐ the written form has not been furnished or does not comply with the Standard.

   ☐ the computer readable form has not been furnished or does not comply with the Standard.

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	
	No:	Claims	1-10,16-19
Inventive step (IS)	Yes:	Claims	
	No:	Claims	1-10,16-19
Industrial applicability (IA)	Yes:	Claims	5-10,16-19
	No:	Claims	

2. Citations and explanations

see separate sheet

III. **Non-establishment of opinion (Continuation)**

Claims 1, 5, 7, 9, 16, 17, and 19 have been searched partially and claims 11-15 have not been searched. The applicant is reminded that claims or parts thereof for which no International Search Report has been established, will not be the subject of the International Preliminary Examination (Rules 66.1 (e); 70.2 (d) PCT). The reasons given by the International Search Authority (ISA) for restricting the search are repeated below:

Present claims 1, 5, 7, and 9 relate to single nucleotide polymorphisms defined by reference to a desirable characteristic or property, namely being associated with a predisposition for accelerated autosomal dominant polycystic kidney disease. The claims cover all single nucleotide polymorphisms having this property, whereas the application provides support within the meaning of Article 6 PCT and disclosure within the meaning of Article 5 PCT for only one of such single nucleotide polymorphisms. In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search over the whole of the claimed scope is impossible. Independent of the above reasoning, the claims also lack clarity (Article 6 PCT). An attempt is made to define the single nucleotide polymorphisms by reference to a result to be achieved. Again, this lack of clarity in the present case is such as to render a meaningful search over the whole of the claimed scope impossible. Consequently, the search and subsequent examination have been carried out for those parts of the claims which appear to be clear, supported and disclosed, namely those parts relating to the Glu298Asp single nucleotide polymorphism in the ENOS gene disclosed in claim 3.

Present claims 16,17, and 19 relate to compounds defined by reference to a desirable characteristic or property, namely having a NO donor or enhancing activity. The claims cover all compounds having this characteristic or property, whereas the application provides support within the meaning of Article 6 PCT and disclosure within the meaning of Article 5 PCT for only a very limited number of such compounds. In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search over the whole

of the claimed scope is impossible. Independent of the above reasoning, the claims also lack clarity (Article 6 PCT). An attempt is made to define the compound by reference to a result to be achieved. Again, this lack of clarity in the present case is such as to render a meaningful search over the whole of the claimed scope impossible. Consequently, the search and subsequent examination have been carried out for those parts of the claims which appear to be clear, supported and disclosed, namely those parts relating to the compounds disclosed on page 16 lines 24-27.

Claims 1-4 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, insofar these claims relate to a method of diagnosis performed on the human or animal body, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(i) PCT).

V. Reasoned statement (Continuation)

2.1 CITATIONS

Reference is made to the following documents:

D1: PERSU A ET AL: 'Modifier effect of ENOS in autosomal dominant polycystic kidney disease.' HUMAN MOLECULAR GENETICS, vol. 11, no. 3, 2002, pages 229-241, XP002220946 1 February, 2002 ISSN: 0964- 6906

D2: WO 01 98286 A (LIN CHIA EN ;GARVEY DAVID S (US); LETTS L GORDON (US); NITROMED IN) 27 December 2001 (2001-12-27)

2.2 MISCELLANEOUS

2.2.1 For the assessment of the present claims 1-4 on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new

medical treatment.

2.3 **NOVELTY (Art. 33(2) PCT)**

2.3.1 D1 which is a journal publication of the applicant discloses methods for diagnosing a predisposition for accelerated autosomal dominant polycystic kidney disease in a human subject by detecting a single nucleotide polymorphism which corresponds to the Glu 298 Asp polymorphism of the ENOS gene. The teaching of D1 therefore falls within the scope of claims 1-10. In view of D1, claims 1-10 are not novel.

2.3.2 D2 discloses the use of pharmaceutical compositions containing L-arginine and a NO donor for treating polycystic kidney disease. The teaching of D2 falls within the scope of claims 16-19. In view of D2, claims 16-19 are not novel.

2.3.3 The present application does not satisfy the criterion set forth in Article 33(2) PCT because the subject-matter of claims 1-10, 16-19 is not novel in respect of prior art as defined in the regulations (Rule 64(1)-(3) PCT).

2.4 **INVENTIVE STEP (Art. 33(3) PCT)**

2.4.1 The present application does not satisfy the criterion set forth in Article 33(3) PCT and the subject-matter of claims 1-10, 16-19 does not involve an inventive step (Rule 65(1)(2) PCT).